Electrophysiological studies on visual information processing in dyslexia and ADHD

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Chapter 2

Distinct information processing characteristics in dyslexia and ADHD during a covert orienting task: An event-related potential study

This chapter was published as: Dhar, M., Been, P.H., Minderaa, R.B., & Althaus, M. (2008). Distinct information processing characteristics in dyslexia and ADHD during a covert orienting task: An ERP study. *Clinical Neurophysiology, 119*, 2011-2025.

Abstract

Objective: A visuo-spatial orienting task was used to investigate the individual and joint contribution of the presence of dyslexia and attention-deficit hyperactivity disorder (ADHD) to information processing.
Methods: Sixteen control, 17 dyslexic, 16 ADHD, and 15 comorbid adults performed the task, comprising a valid, invalid, and no-cue condition. Performance measures were errors and reaction time (RT). A negative potential in response to cues and targets (N2), and a positive potential in response to targets (P3) were derived from the EEG. A 2 x 2 design was used with the factors dyslexic/non-dyslexic, and ADHD/non-ADHD.
Results: Dyslexic participants demonstrated a smaller cue-related N2, yet a greater target-related N2 in the valid condition. ADHD participants were discriminated by the P3 difference between the invalid and valid condition. Comorbids differed from ADHD mainly in invalid-valid RT, and were similar to dyslexics in target N2 processing.
Conclusions: Dyslexics were impaired in early information processing, and participants with ADHD differed for later processing stages.
Significance: This is the first ERP study of attentional processes in dyslexia to incorporate an ADHD and a comorbid group. Its results may contribute to differentiation of these clinical groups.

Introduction

Dyslexia is a neurologically-based disorder in learning to read. Though it is widely accepted that dyslexia encompasses a deficit in phonological processing, it has been established that visual attentional processing affects reading performance as well as phonological processing (Eden et al., 1996; Facoetti et al., 2006; Kinsey et al., 2004; Valdois et al., 2004).

Dyslexia often co-occurs with attention-deficit hyperactivity disorder (ADHD), which is a neurodevelopmental disorder that can cause impulsiveness, hyperactivity and attentional dysfunction (American Psychological Association [APA], 2000). Like dyslexia (Bruck, 1998; Shaywitz et al., 1998), ADHD not only affects children; in roughly half of the children diagnosed with ADHD, symptoms persist into adulthood (Biederman, 1998; Spencer et al., 1998). The co-occurrence raises questions as to how the disorders interact and in which respect (also to what extent) they can be differentiated. As visual attentional problems play a significant role in both disorders, understanding the mechanisms underlying these deficits may help in differentiating the disorders. Comorbidity is also important for understanding research data on dyslexia, as findings have been confounded by ADHD factors. Yet most studies have not taken the co-occurrence of dyslexia and ADHD into account.

Reading is an automatised process that enables us to rapidly and covertly shift our attention across a sentence before a saccade is actually made. Directing attention is therefore an essential component of reading (Casco et al., 1998). During reading, information processing can be enhanced at a spatial location through feedback from the dorsal to the ventral pathway of the visual system (Van der Heijden, 1992). The dorsal part of the visual system, or the "where" system, is sensitive to the location of an object, whereas a second system, the ventral or "what" visual system is responsible for processing features such as shape and colour (Mishkin et al., 1983). Due to dysfunction of the "where" system, dyslexic individuals may be less capable of directing spatial attention and consequently of controlling visual input while reading (Vidyasagar, 2004).

Indeed, impairments in visual perception and processing in dyslexia have been found that were explained in terms of deficient dorsal system functioning (Lovegrove et al., 1990; Stein & Walsh, 1997; Shaywitz et al., 2002). Attentional difficulties have been found in dyslexics, including asymmetric control of visual attention (Facoetti et al., 2001; Hari et al., 2001), slower visual search speed (Iles et

al., 2000), and problems in focusing attention (Facoetti et al, 2000; Geiger & Lettvin, 1987; Rayner et al., 1989).

Consequently, the present study will focus on processes of visual attention that rely on posterior brain systems. The Posner spatial cueing task, in which a spatial cue is followed by a target, is considered to be effective for this purpose (Posner & Petersen, 1990). In this task a cue is used to direct covert attention to a certain location. If the cue is presented peripherally and is followed by a target after an interval shorter than 300 ms, the cue evokes an automatic covert orienting reaction to the target location (Jonides, 1981; Posner & Petersen, 1990). Automatic, involuntary orienting has been associated with posterior brain areas, including the superior parietal lobe and temporal parietal junction (Corbetta & Shulman 2002; Karnath et al. 2001; Posner & Petersen, 1990).

Using performance measures, some evidence has been found on tasks of this kind for a weaker automatic orienting of visuo-spatial attention in dyslexia. Brannan and Williams (1987) showed that dyslexic children were less capable of using a peripheral cue to rapidly shift attention. In their studies on covert orienting of attention in dyslexia, Facoetti and co-workers (2000) found that dyslexics could efficiently allocate voluntary attention to a spatial location, but when a short stimulus onset asynchrony (SOA) was used to elicit an involuntary orienting response, reaction times were markedly slower than in controls.

On a biological level, post-mortem examinations on dyslexic brains have led to the discovery of microscopic lesions (ectopias, microgyria, and reduced diameter of visual magnocells) in cortical areas and thalamic nuclei, including the right temporoparietal junction (Galaburda & Kemper, 1979; Galaburda et al., 1985; Kaufmann & Galaburda, 1989). In line with this, functional magnetic resonance imaging (fMRI) studies on dyslexia have found deficits related to the posterior parietal and temporoparietal cortex (Eden & Zeffiro, 1998; Shaywitz et al., 2002). For a review of fMRI results see Grigorenko, 2001.

In children and adults with ADHD, performance decrements on visuo-spatial orienting tasks have also been found (Swanson et al., 1991; Epstein et al., 1997). However, in contrast to dyslexia, most evidence has been found for impairments in voluntary allocation of visuo-spatial attention, whereas automatic orienting to exogenous cues seems to be intact, according to a meta-analysis by Huang-Pollock and Nigg (2003). ADHD is thus associated with deficits in more frontally mediated functions. MRI studies on ADHD suggest structural

abnormalities of the frontal and anterior cingulate cortex as well as basal ganglia nuclei (for a review see Willis & Weiler, 2005).

Most studies on orienting of attention in dyslexia and ADHD have been conducted using performance measures only. Using ERP has the added benefit of investigating the neurocognitive process that take place before an overt response is given. Thus, it provides the possibility to isolate earlier and later information processing stages that may reveal group differences, not apparent at a performance level. For example, using performance measures only, Willcutt and others (2005) found slow and variable RT to be a common characteristic of children with dyslexia, ADHD, and comorbid children.

A component frequently studied in ERP research on visual processing is the N2, a negative deflection that peaks around 200 ms following a stimulus. The N2 has been related to stimulus identification and stimulus conflict (Nieuwenhuis et al., 2004). Generally, in ADHD, attenuated posterior N2 peaks have been associated with a dysfunction in discriminating or identifying task-relevant stimuli (Karayanidis et al., 2000). Visual N2 abnormalities in dyslexia have been found (Casarotto et al., 2003), but not consistently (Rüsseler et al., 2003).

Another component, the P3, which reaches a parietal maximum between 300 and 700 ms after onset of a relevant and/or salient stimulus, is said to reflect context updating, and has often been used as a measure of conscious, controlled attention allocation (Donchin & Coles, 1988), and effortful processing (Kok, 2001). Although the P3 has been said to be generated by widely distributed sources, it is currently believed that the P3 is generated at the temporoparietal junction (Hruby & Marsalek, 2003; Nieuwenhuis et al., 2003). Smaller P3s have been found in children with dyslexia (e.g. Holcomb et al., 1985), but not consistently (Stelmack et al., 1988). The same holds for ADHD, for which results have been inconsistent (Wiersema et al., 2006; for a review see Barry et al., 2003).

The ERP methodology has successfully been applied to the covert orienting paradigm (Curran et al., 2001; Eimer, 2000; Fu et al., 2001; Nobre et al., 2000; Yamaguchi et al., 1994). On this task, the N2 has been found to have a larger amplitude and longer latency to invalidly cued targets vs. validly cued targets (e.g. Perchet & Garcia-Larrea, 2005). Also, the P3 has been found to be larger and has a later onset on invalid trials (e.g. Wright et al, 1995). The right temporoparietal junction has been implicated in reorienting to unattended stimuli in the invalid task condition and target detection (Corbetta et al., 2000; Astafiev et al., 2006; Thiel et al., 2004).

As of yet, relatively few ERP studies have addressed orienting of visual attention in children or adults with dyslexia and/or ADHD. Jonkman and others (1992) found no differences between controls and children with dyslexia. Wijers and colleagues (2005) discovered that, contrary to reaction time studies reporting impairments in processing of left visual field stimuli, dyslexic adults showed impaired performance to stimuli in both visual fields and aberrant symmetry of attentional processing.

The only ERP study of comorbid dyslexia and ADHD in adults was conducted by Duncan and colleagues (1994). They divided their group of male dyslexic adults into a high ADHD and a low ADHD group based on self-reported symptoms of ADHD in childhood. Three visual tasks were used with varying task demands. The smaller P3 found in men with dyslexia on the high-demand task was attributed entirely to the presence of ADHD symptoms. However, this study did not use a group of men formally diagnosed with ADHD.

The present study aims to differentiate the attentional processes that may underlie deficiencies in reading by utilising the Posner covert orienting paradigm with short SOAs and non-predictive peripheral cues in adults with a formal DSM-IV-TR diagnosis of ADHD and/or with dyslexia. The ERPs in response to cue and target will be examined for early mechanisms involved in automatic orienting to a spatial location, and later mechanisms involved in consciously controlled effortful processing. The N2 evoked by the cue will provide information about the system's automatic orientation to a visual stimulus. The N2 in response to a target, on the other hand, will provide information about how participants discriminate targets, validly and invalidly cued. When targets are invalidly cued, there is a conflict between cue and target, thus the N2 is expected to be enhanced compared to the valid condition. The target P3 will give insight into processes involving conscious evaluation of the stimulus and attention allocation.

In addition, the hemispheric distribution of activation will be studied to gain insight into the hemispheric lateralisation of processing. Because we expect there to be functional differences in brain topography between the groups, sources of activity will be estimated with Low Resolution Electromagnetic Tomography, or LORETA (Pascual-Marqui & Lehmann, 1994).

We expect dyslexic participants to show early processing deficits caused by problems with the posterior attention network. ADHD participants are expected to show more problems with controlled processes indexed by the P3. Because gender differences on visual attention tasks have been found for dyslexia

(Bednarek et al., 2004) and ADHD (Swanson et al., 1991), this study will focus solely on men with dyslexia and ADHD.

Materials and methods

Participants

Eighteen male participants with dyslexia (mean age = 35.2 years; SD = 8.7), 16 males with ADHD (mean age = 33.1 years; SD = 8.5), 15 male participants with both dyslexia and ADHD (mean age = 35.9 years; SD = 8.2) and 16 male controls (mean age = 33.7 years; SD = 8.9) took part in the study. The age range of participants was 19 to 49 years. Participants were matched for age and handedness, which was determined by means of a checklist (Van Strien, 1982). Exclusion criteria for all participants were: history of brain-related illness, diagnosed neurological disorder other than dyslexia or ADHD, and estimated IQ below 85. Intelligence was assessed with an abbreviated version of the Groninger Intelligentie Test (GIT) (Luteijn & Van der Ploeg, 1983). Mean IQ for dyslexia was 111.2 (SD 9.4), the ADHD group 110.3 (SD 9.6), the comorbid group 109.8 (SD 10.2), and controls 116.4 (SD 9.4). No statistically-significant difference in IQ was found. All participants had normal or corrected-to-normal vision. Participants were recruited through a newspaper advertisement and through patient support groups. Furthermore, a number of dyslexic and control participants were recruited from the Dutch Longitudinal Study of Dyslexia.

All the participants with ADHD had sought help from mental health services and consequently had been formally diagnosed according to DSM-IV-TR criteria for ADHD by clinical experts. To gain insight into symptoms of ADHD in childhood and adulthood, the participants completed a self-report scale based on the DSM-IV-TR criteria (Kooij et al, 2004). The scale was completed by all but three participants who were not able to remember their behaviour as a child. These three people however did score above the 95 percentile on the ADHD scale of the Adult Self Report (ASR) (Achenbach & Rescorla, 2003), which was completed by all participants, and was used to screen for potential behavioural problems.

All participants were screened for the presence of dyslexia. To this end, two standardised Dutch reading tests were used: the EMT (Eén Minuut Test: One Minute Test), which is a single word reading test (Brus & Voeten, 1972), and the KLEPEL, a pseudoword reading test (Van den Bos et al., 1994). For inclusion in the dyslexic group one of three criteria had to be met. 1) EMT or KLEPEL reading

score had to be below the 11th percentile. 2) Both had to fall within the lowest quartile. 3) Percentile score of the verbal comprehension minus percentile score for pseudoword reading had to be greater or equal to 60. This criterion is based on a discrepancy between reading achievement and IQ which is important for discerning readers who are average on the reading tests but poorer than would be expected based on intelligence (Scarborough, 1989; APA, 2000). Verbal comprehension was measured using a subtest of the Wechsler Adults Intelligence Scale-III (WAIS-III) and had to be above the 15th percentile. The dyslexic adults who were recruited from the Dutch Longitudinal Study of Dyslexia had been previously screened for dyslexia and were consequently not screened again. For inclusion in the comorbid group, participants had to meet criteria for both ADHD and dyslexia.

Adults were included in the control group, provided there were no reading problems on the dyslexia screening tests or behavioural problems. All controls fell within the normal range of the ASR and ADHD rating scale.

Tasks and stimuli

Subjects were seated approximately 60 cm from a computer screen. Each task trial consisted of a centrally located fixation dot presented for 1000 ms followed by a peripheral cue that appeared to the left or the right of fixation and subsequently a target, which was a dark letter, appearing on a light background. Stimuli were presented at 1° from central fixation, which remained visible during the task. Both cue and target duration was set at 50 ms with a SOA of 200 ms. The cue could be valid, i.e. predicted target location correctly, or invalid; the target appeared in the opposite visual field. However, the target was cued on only two thirds of the trials. On the remaining trials (neutral condition), only a target was presented. The target letter could be either “O” or “X”. Each trial type was randomly presented 50 times. The participant was required to press, as quickly as possible, a left button with the left hand in response to the letter “O” and a right button with the right hand in response to the letter “X”.

Procedure

The study protocol was approved by a medical ethics committee. All participants were required to give informed consent before the experiment began. Participants with ADHD refrained from using psychostimulant medication (methylphenidate) 24 hours before taking part in the experiment.

Experiments took place in an EEG laboratory at the Neuroimaging Center of the University Medical Center in Groningen, The Netherlands. Prior to the EEG session the dyslexia test and the abbreviated intelligence test were administered. During the EEG session participants were seated in a sound-attenuated EEG chamber, devoid of distracting stimuli under low illumination. The experimenter was seated in the control room and was able to monitor the participant throughout the EEG session. The experimenter was not visible to the participant during experimentation. Each task was preceded by a practice session. After each practice session, it was verified that the participant understood the task before starting the experiment. The described task was part of a larger study investigating a variety of information processing capacities in participants with dyslexia and ADHD. Only the task relevant to the present study on visuo-spatial orienting will be reported in this article.

Overt performance

Performance measures were response accuracy, mean reaction time (RT) to targets, and within-subject variability of RT (SD-RT). Mean RT was calculated from correct trials only. Responses before 250 ms or 1500 ms after target offset were considered invalid as well as incorrect responses and omissions.

Electrophysiological recording and analysis

Continuous EEG was sampled using a SynAmps model 5083 amplifier (Neuroscan) with an input impedance of 10 MOhm, from 72 Ag/AgCl-sintered ring electrodes embedded in an EEG recording cap made by EASYCAP GmbH at 500 Hz. Such a large number of electrodes were used to assure a reliable resolution for the LORETA analyses. Reference electrodes were attached to the mastoids. A ground electrode was placed on the right cheekbone. Electrodes were arranged according to the international 10/20 system (Jasper, 1958). Horizontal electro-oculogram (EOG) was recorded from the outer canthus of each eye. Vertical EOG was recorded from infraorbital and supraorbital electrodes placed in line with the pupil of the left eye. Electrodes were filled with conductive gel using a syringe without a needle. Cotton buds were used to ensure that the impedance was kept below 15 kOhm. With an input impedance of the amplifier as high as 10MOhm, there was no need to reduce electrode impedance any further (Ferree et al., 2001). A band-pass filter (0.5 – 30 Hz, 48 dB/oct) and notch filter (50 Hz) were applied to

the raw data. The Gratton and Coles algorithm (Gratton et al., 1983) was used to correct vertical and horizontal eye movements.

Only trials with a SOA of 200 ms were used for ERP analyses. The performance data from the no cue condition were analysed, however the ERP data from this condition were left out of the analysis for the following reason. In cued conditions the waveform of the target was influenced by the cue-related activity. Because there was no cue prior to the target in the neutral condition, the uncued target waveform could not be compared to the cued target waveform. In other words, evoked potentials in an S1 - S2 paradigm cannot be compared with ERPs derived from a single stimulus paradigm.

The filtered EEG was segmented twice for different purposes. Initially, in order to analyse cue-related activity, signals were segmented from 200 ms before to 800 ms after cue onset to create a window encompassing both cue and target processing. Cue-locked averages were then computed with a baseline of 200 ms preceding cue onset. Prior to averaging, segments containing activity above 75 μV or below -75 μV were considered artefacts and were rejected. Averages were based on correct responses only. Next, a window for cue N2 peak detection (180-225 ms) was determined based on visual inspection of grand averages. Peak amplitudes as well as latencies were analysed.

The second segmentation was performed in order to obtain reliable identification of target-related activity. The baseline was determined through inspection of grand averages over a large time domain, which showed that target-related activity had diminished before 1200 ms justifying the choice for a baseline from 1200 to 1400 ms. Artefact rejection was performed in the same manner as above and then target-locked averages were calculated. Windows for peak detection were based on inspection of grand averages and cortical mappings of brain activity. The target N2 was defined as the most negative peak in the 185-245 ms interval after target onset. Again, the peak amplitudes and latencies were entered in the analysis.

The P3 emerged as a somewhat longer lasting parietal complex 300-500 ms after target onset. To gain insight into the processes underlying this complex we segmented an interval from 300 to 500 ms into 50 ms bins for which mean amplitudes were computed (Handy, 2005). Only correct trials were used to calculate averages.

To gain further insight into the topographical distribution of cortical activation during detection of the cue, sources were estimated by analysing the

maximum current density with LORETA. For theses analyses, the baseline correction was removed from the grand averages, and the ERPs were transformed to the averaged reference. Next, the current density was plotted in the time frame corresponding with the maximum amplitude of the cue.

Statistical analyses

Data analyses occurred in three steps.

Step 1: Factorial design.

In order to finally conduct comparisons on a reduced number of variates, we first adopted a 2 x 2 factorial design, with ADHD (ADHD vs. non-ADHD), and dyslexia (dyslexic vs. non-dyslexic) as independent variables. This two-way design allowed us to investigate the individual and interactive effects of ADHD, and dyslexic problems on the dependent variables (Stevens, 1999). For this reason this design has frequently been employed in research on the co-occurrence of dyslexia and ADHD (e.g. McGee et al 2000 and 2004; Purvis & Tannock, 2000; Tiffin-Richards et al., 2004; Willcutt et al., 2001 and 2005). For analyses of the performance data, this design comprised the within-subject variables: cue-validity (neutral vs. valid vs. invalid), and visual field (left vs. right). Different runs were conducted for the dependent variables, which were percentage of errors, mean RT, and SD-RT.

For the statistical analyses of ERP data, dependent measures were peak amplitudes and latencies of the cue N2, and target N2. For analysis of the P3, mean amplitudes of the P3 bins were entered. Within-subject factors were cue position (with two levels: left visual field vs. right visual field), target position, only for target-related components (with two levels: left visual field vs. right visual field), hemisphere (with two levels: left hemisphere electrodes vs. right hemisphere electrodes) and electrode site. Electrode sites for the cue and target N2 were confined to parietal and occipital electrode positions (P1/2, P3/4, P5/6, P7/8, P9/10, PO3/4, PO7/PO8, PO9/10, O1/2, O9/10), as we were interested in visual attentional processing mediated by the posterior attention network. For the P3 bins central-parietal electrodes sites were analysed (CP1, CP2, CP3, CP4, CP5, CP6, P1, P2, P3, P4, P5, P6, P7, P8). First, an ANOVA was conducted on the defined cluster of electrodes, then a second ANOVA was conducted for the electrode pair with the highest amplitude/longest latency. Laterality (hemisphere) was taken into account, as stimuli were presented in left and right visual field causing higher amplitudes in

the opposite hemisphere. The interaction between cue and target position signified the validity effect. Concerning the P3 bins, to prevent capitalisation on chance, an effect was accepted only if two subsequent bins showed significance.

Step 2: Group comparisons.
To investigate differences between participant groups we performed a multivariate analysis of variance (MANOVA) with the between subjects variable group, consisting of the four participant groups, while entering into the design the dependent variables that were shown to be significantly affected by ADHD and/or dyslexia problems, i.e. those variates for which significant (interaction) effects were found in the analyses of step 1. Interaction effects with one or more of the within-subject variables entered in the step 1 analyses were accounted for by computing a variable reflecting this effect, e.g. if there was an ADHD by validity interaction for the P3 amplitude, we subtracted the mean amplitude of the valid condition from that of the invalid condition. Variables revealing a significant main effect of the factor group were submitted to pairwise comparisons while applying the Tukey HSD correction for capitalising on chance.

Step 3: Discriminant function analysis.
Finally, a discriminant function analysis was conducted on the groups in order to explore which combination of measures that were previously shown to be differentially affected by the groups, best distinguished the participant groups.

All hypotheses were tested against a .05 significance level. In cases of non-sphericity, degrees of freedom were corrected with the Greenhouse-Geisser epsilon coefficient in the MANOVAs.

One participant was left out of the analyses because not enough trials were left after artefact rejection. In another participant, two electrodes were not measured due to a technical error. Nevertheless, data from this participant were included in the analyses for the remaining electrodes.

Results

Step 1: Factorial design

Performance data

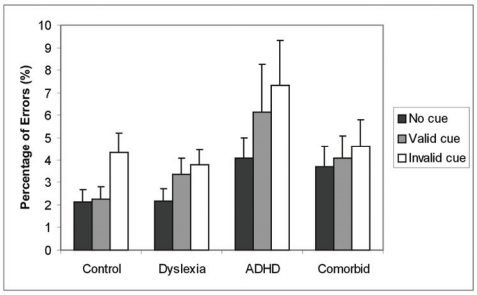

Figure 1. For each group, percentage of errors is shown for the three cue conditions: no cue (black), valid cue (grey) and invalid cue (white).

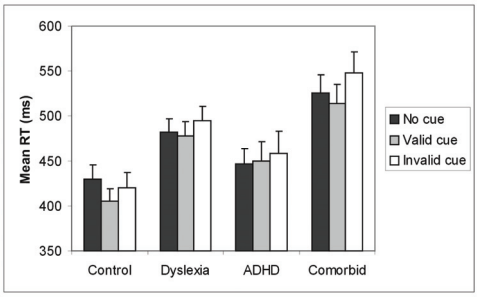

Figure 2. Mean RT in ms is depicted per group for each cue condition. Cue conditions are represented by colours: no cue (black), valid cue (grey) and invalid cue (white).

Accuracy

Figure 1 shows the mean percentage of errors per participant group for the three validity conditions. There is a main effect for validity, with most errors in the invalid condition ($F(2,59) = 8.18$, $p = .001$), and a main effect for the factor ADHD ($F(1,60) = 4.11$, $p = .047$), indicating that the presence of ADHD contributes to an increase in errors.

RT

In Figure 2, mean RT is depicted for each participant group. There are main effects for both factors dyslexia and ADHD (dyslexia: $F = 15.82$, $p < .001$, ADHD: $F = 4.52$, $p = .038$), demonstrating that the factors ADHD and dyslexia contribute independently to an increase in RT. When valid trials are contrasted with invalid ones, the factor dyslexia contributes to a greater cost in the invalid condition (see Figure 2), resulting in a significant validity x dyslexia interaction, ($F(1,60) = 6.41$, $p = .014$). A dyslexia x ADHD x validity interaction ($F(1,60) = 4.24$, $p = .044$), suggests that the presence of ADHD and dyslexia contribute interactively in the effect of validity on RT.

SD-RT

Figure 3 depicts the variability in RT for each participant group for the three validity conditions. There are validity independent main effects for the factors dyslexia and ADHD: dyslexia, $F(1,60) = 5.28$, $p = .025$; ADHD, $F(1,60) = 9.00$, $p = .004$, demonstrating that these factors contribute independently to the increase in RT variability. Moreover, a trend to significant dyslexia x validity interaction reveals that participants with dyslexia (dyslexic and comorbids) have a tendency to

react more variably in the invalid condition in comparison with the valid condition ($F(1,60) = 3.42$, $p = .069$). A dyslexia x ADHD x validity interaction ($F(1,60) = 5.10$, $p = .028$), suggests that the expression of SD-RT is dependent on the differential contribution of dyslexia and ADHD to cue validity (see Figure 3).

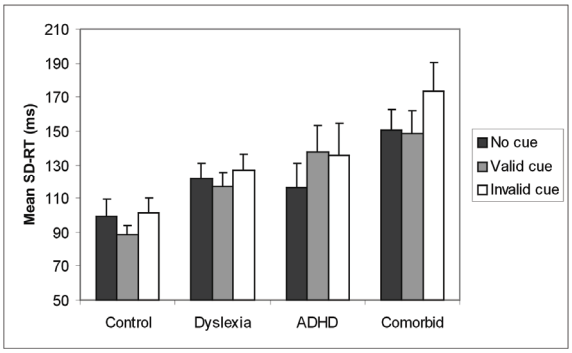

Figure 3. Mean response variability (SD-RT) in ms for all groups in the three cue validity conditions independent of visual field.

Electrophysiological measures

Cue processing - N2

Latency

For cue N2 latency, a cue position x hemisphere interaction was found ($F(9,51) = 21.99$, $p < .001$), when entering the following electrodes (P1/2, P3/4, P5/6, P7/8, P9/10, PO3/4, PO7/PO8, PO9/10, O1/2, O9/10). Left visual field cues were processed later in the right hemisphere than in the left hemisphere and vice versa. The interaction differed for electrode site resulting in the three-way interaction, cue position x hemisphere x electrode, showing that the effect is most pronounced for P7 and P8 ($F(1,60) = 362.87$, $p < .001$). No effects of ADHD and/or dyslexia were found for cue N2 latency.

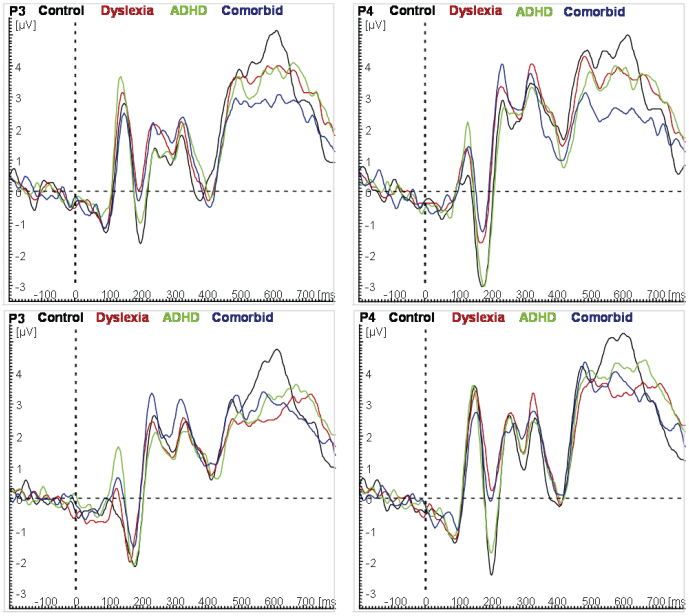

Figure 4. Cue-locked grand averages for left (top) and right (bottom) cues at P3 and P4. Groups are represented by colours. Cue N2 amplitude is maximal at approximately 200 ms.

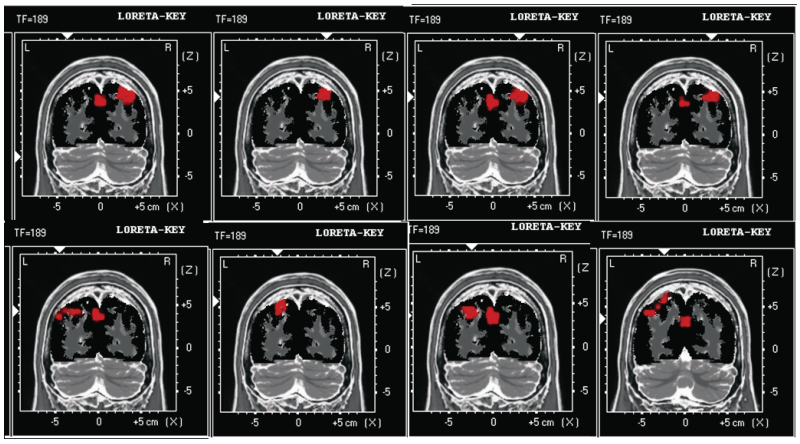

Figure 5. Low-resolution electromagnetic tomography analysis (LORETA) maps of neural activity corresponding with the cue N2. Top panel represents activity to left cues and bottom panel represents activity to right cues. Groups from left to right: control, dyslexia, ADHD and comorbid. Activation is present in the left superior parietal lobe (LSPL) corresponding to electrode P3, right superior parietal lobe (RSPL) corresponding to electrode P4, and precuneus corresponding to POZ. See Table 1 for absolute maxima.

	Control		Dyslexia		ADHD		Comorbid	
	L cue	R cue	L cue	R cue	L cue	R cue	L cue	R cue
LSPL	-	2.48	-	1.89	-	2.48	-	1.80
RSPL	3.70	-	2.39	-	2.43	-	2.00	-
Precun	2.65	2.28	1.40	1.20	2.00	1.90	1.55	1.77

Table 1. Maximum current densitiy (x 10^2) in the left superior parietal lobe (LSPL), right superior parietal lobe (RSPL) and precuneus (Precun) for left and right cues in each group.

Amplitude

There was a significant cue position x hemisphere x electrode interaction in the whole parieto-occipital region (same electrodes as above: $F(9,51) = 10.99$, $p < .001$), revealing the strongest effects for P3 and P4, ($F(1,60) = 27.64$, $p < .001$), as depicted in Figure 4. Participants with dyslexia (dyslexic and comorbid) demonstrated cue position independent smaller N2 amplitudes on the same cluster of parieto-occipital electrodes as mentioned above, compared to participants without dyslexia (controls and ADHD). This main effect for dyslexia ($F(1,59) = 5.83$, $p = .019$) was again greatest at P3/4, ($F(1,60) = 7.17$, $p = .01$). Moreover, N2 amplitudes were smaller in the right hemisphere in participants with dyslexia (dyslexic and comorbid) compared to non-dyslexic participants (controls and ADHD), causing a hemisphere x dyslexia effect (P3/4: $F(1,60) = 4.16$, $p = .046$).

LORETA was used to visualise the areas active during detection of the cue. In corroboration of the task manipulation, the superior parietal lobes contralateral to the cues were found to be active in the time frame corresponding with the cue N2 peak latency at P3 and P4, for which the previously described main dyslexia effect was found. In addition, we found a parietal area at the midline (precuneus) to be activated that corresponded with the electrode position POZ. This finding led to an additional analysis of the cue N2 at POZ, corresponding with the position of the precuneus, and produced a yet greater main effect for the factor dyslexia ($F(1,60) = 8.68$, $p = .005$). The results of the LORETA analysis are presented in Table 1, depicting the maximum current density at the left and right superior parietal cortex and precuneus. Figure 5 shows activation predominantly in the superior parietal lobe in the hemisphere contralateral to the cue, and activity in the precuneus, which is suggested to be lower.

Target processing - N2

Latency

For target N2 latency, a target position x hemisphere interaction ($F(1,59) = 78.50$, $p < .001$) was found once again in the whole parieto-occipital region (P1/2, P3/4, P5/6 P7/8, P9/10, PO3/4, PO7/8, PO9/10, O1/2, O9/10). A hemisphere x target position x electrode interaction, ($F(1,59) = 8.00$, $p < .001$) revealed that the effect was strongest for PO7/8 ($F(1,60) = 94.24$, $p < .001$). A cue position x target position x ADHD interaction at PO3/4 ($F(1,60) = 8.66$, $p = .005$), showed that participants without ADHD (controls and dyslexics) displayed longer N2 latencies to invalid targets than to valid targets, whereas participants with ADHD (ADHD and comorbids) displayed longer N2 latency for valid targets than for invalid targets.

Amplitude

Analysis of the target-locked N2 amplitude did not result in an overall validity effect in the parieto-occipital region (see above). Yet, there was a validity effect for the factor dyslexia (cue position x target position x dyslexia: $F(9,59) = 10.50$, $p = .002$), which was largest at P5/6 ($F(1,60) = 12.50$, $p = .001$). Figure 6 shows grand averages for electrodes P5 and P6. A four-way interaction demonstrated that this validity effect was dependent on hemisphere, cue position x target position x hemisphere x dyslexia ($F(1,60) = 4.83$, $p = .032$), with dyslexics (dyslexia and comorbid participants) showing a larger N2 in the right hemisphere on valid trials.

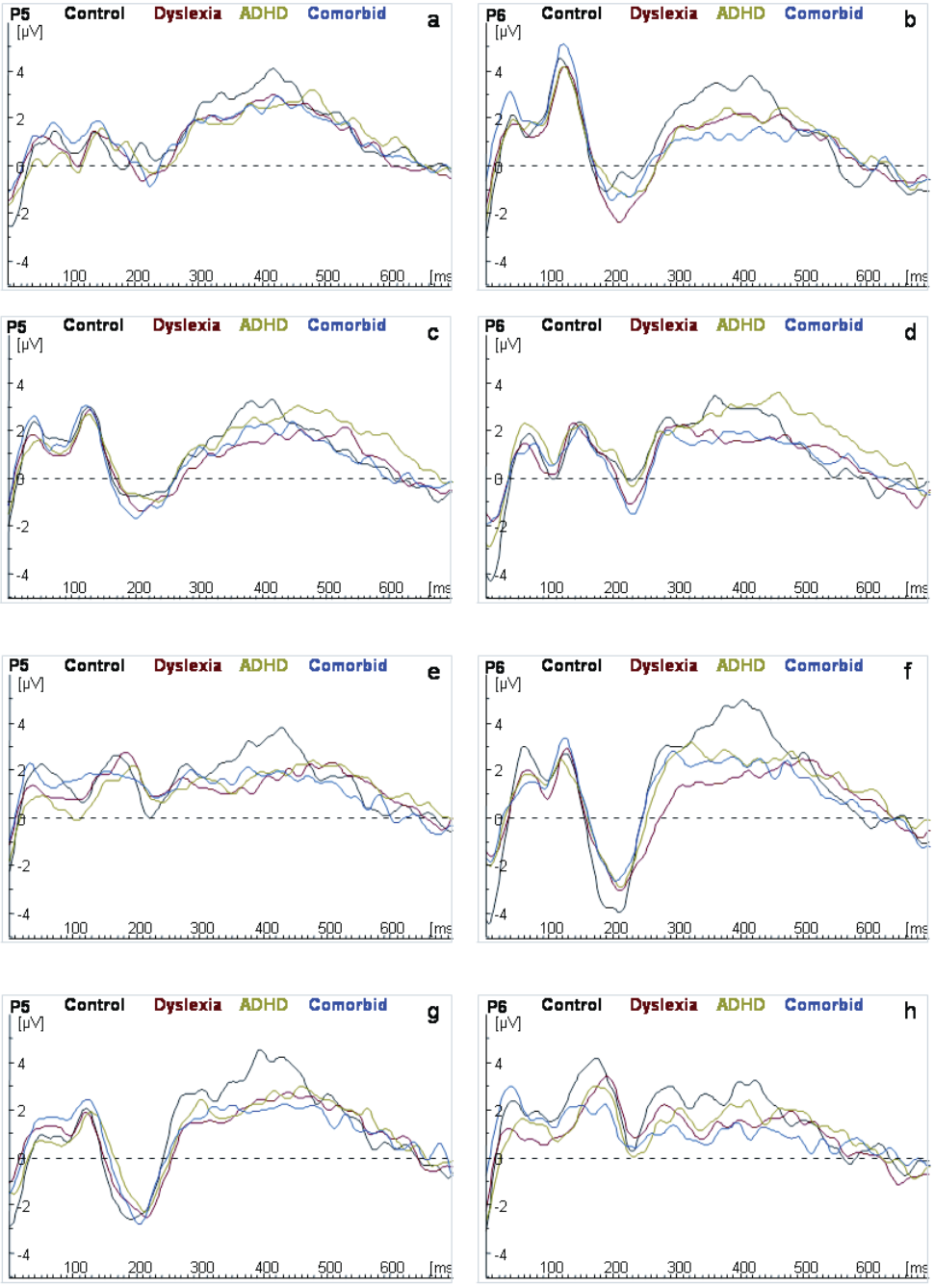

Figure 6. Target-locked grand averages for N2 measured at P5 and P6. From top to bottom, left valid (a + b), right valid (c + d), left invalid (e + f) and right invalid (g + h) conditions are depicted. Groups are represented by colours: controls group (black), dyslexic group (red), ADHD group (green) and comorbid group (blue).

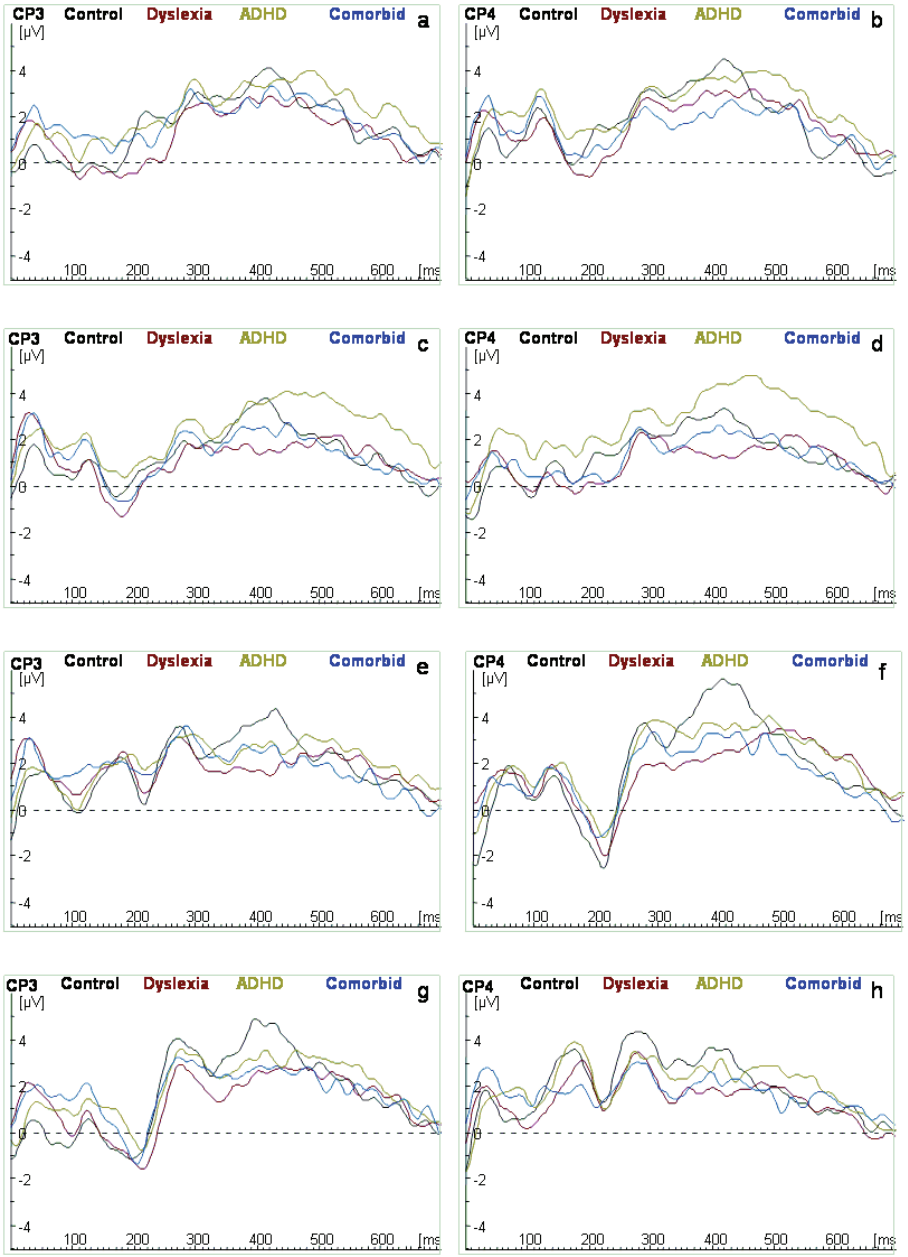

Figure 7. Target-locked grand averages for P3 at CP3 and CP4. From top to bottom, left valid (a + b), right valid (c + d), left invalid (e + f) and right invalid (g + h) conditions are shown. Groups are represented by colours: controls group (black), dyslexic group (red), ADHD group (green) and comorbid group (blue).

Target P3

Mean area of the P3 bins was analysed per 50 ms bin from 300 to 500 ms. The largest effects were found in bins 3 and 4 (350 to 450 ms) at sites P7/8 and CP3/4. P3 amplitude for left visual field targets was greater in the right hemisphere and vice versa (CP3/4: hemisphere x target position for the 350 to 400 ms bin: $F(1,60) = 17.13$, $p = .001$ and the 400 to 450 ms bin: $F(1,60) = 30.57$, $p = .001$). A hemisphere x dyslexia interaction revealed that the presence of dyslexia coincided with smaller mean P3 amplitudes in the right hemisphere (P7/8: hemisphere x dyslexia bin 2: $F(1,60) = 4.35$, $p = .041$, bin 3: $F(1,60) = 6.61$, $p = .013$). A four-way cue position x target position x dyslexia x ADHD interaction found from 350 to 450 ms (bins 3 and 4) was most significant for CP3/4 (bin 3: $F(1,60) = 8.11$, $p = .006$, bin 4: $F(1,60) = 5.13$, $p = .027$). The factors dyslexia and ADHD differentially contributed to the P3 depending on the validity condition, as illustrated by the grand averages of CP3 and CP4 (see Figure 7).

Step 2: Group comparisons: MANOVA

The previous ANOVAs revealed significant (interaction) effects of dyslexia and/or ADHD for mean percentage of errors, mean invalid – valid RT (ΔRT), mean SD-RT, mean cue N2 at POZ, mean invalid – valid target N2 at P5/6 (ΔtargetN2), and mean invalid – valid P3 in bin 3 at CP3/4 (ΔP3). These were entered in a MANOVA with the groups representing the four levels of the between-subjects factor group, resulting in an overall main effect for group ($F(15,174) = 4.08$, $p < .001$), and significant group effects on the following variates: ΔRT ($p < .015$), mean SD-RT ($p < .005$), cue N2 ($p < .018$), ΔtargetN2 ($p < .005$), and ΔP3 ($p < .04$). No group effect was found for percentage of errors.

Pairwise group comparisons (Tukey-corrected) revealed several significant differences. Controls and dyslexics differed for cue N2 ($p < .02$) and Δtarget N2 ($p < .02$). Controls differed from ADHD participants in ΔP3 ($p = .028$) and from comorbid participants in Δtarget N2 ($p < .02$) and mean SD-RT ($p < .003$). ADHD participants furthermore differed marginally from dyslexics in cue N2 ($p < .057$) and from comorbid participants in ΔRT ($p < .013$). This allowed us to conduct a discriminant function analysis.

Step 3: Discriminant function analysis

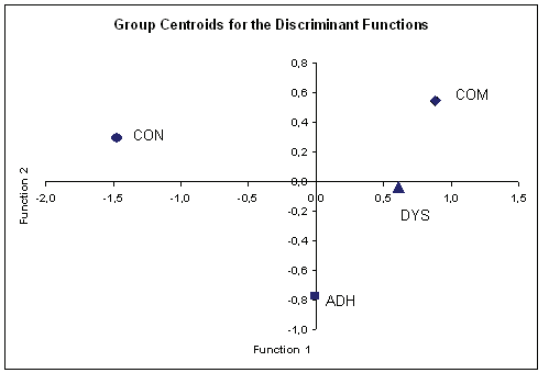

Figure 8. Group centroids of the discriminant functions are shown for Function 1 (x-axis) and Function 2 (y-axis).

		Predicted Group Membership				
	Group Member-ship	Control	Dyslexia	ADHD	Co-morbid	Total
Count	Control	11	0	4	1	16
	Dyslexia	2	8	2	5	17
	ADHD	3	0	13	0	16
	Comorbid	2	3	1	11	15
Percent	Control	68.8	0	25.0	6.3	100
	Dyslexia	11.8	47.1	11.8	29.4	100
	ADHD	18.8	0	81.3	0	100
	Comorbid	13.3	6.7	6.7	73.3	100

Table 2. Results of the discriminant function analysis. Number and percentage of predicted cases are depicted.

The variables that produced significant group contrasts were entered into the discriminant function analysis. The analysis resulted in three functions, two of which had significant values of Wilks' λ (χ^2 = 56.97, *df* = 15, p < .001; and χ^2 = 20.05, *df* = 8, p < .010), indicating that they yielded significant group differences. The first function was guided by mean Δtarget N2, SD-RT, and cue N2. Correlations between these variables and the discriminant functions were respectively .51, .45, and .35. The second function consisted primarily of ΔP3, and ΔRT. For these variables, correlations with the second function were respectively .68 and .67. Figure 8 displays the group centroids for the discriminant functions, showing that Function 1 discerned controls from comorbid participants with mean SD-RT and Δtarget N2, controls from dyslexics with cue N2 and Δtarget N2, and ADHD marginally from dyslexics by cue N2. Function 2 dissociated ADHD from comorbid participants with ΔRT, and from controls with ΔP3. See above for significance levels. Application of the discriminant function resulted in accurate classification for 67.2% of the cases (control: 68.8%, dyslexia: 47.1%, ADHD: 81.3%, comorbid: 73.3%). The resulting classification is depicted in Table 2.

Summary of the main findings

The factor dyslexia led to slower and more variable responses, attenuated N2 amplitudes to cues, especially at POZ, larger target N2 amplitudes to valid targets, specifically in the right hemisphere, but smaller P3s in the right hemisphere.

ADHD caused responses to be slower, more variable, and more inaccurate. Moreover, target N2s had a longer latency to validly cued targets, and the P3 was larger in the valid condition.

Finally, group analyses discriminated the groups by performance and ERP measures, with dyslexics being identified by mainly cue and Δtarget N2, ADHD by ΔP3, and comorbids by a combination of SD-RT, ΔRT and Δtarget N2.

Discussion

The main aim of the present study was to investigate how dyslexia and ADHD individually and interactively contribute towards early and late attentional processes involved in the performance of a visuo-spatial orienting task. To this end, a 2 x 2 factorial design was used. Four groups were included, i.e. a group with 1)

dyslexia, 2) ADHD, 3) dyslexia and ADHD and 4) a control group. First, we will discuss performance and ERP findings, and subsequently limitations and future directions will be considered.

There were differential group effects of cue validity on RT and variability of RT. Dyslexics exhibited a slower RT in general and a greater cost to invalidly cued targets than non-dyslexics, indicating the need for more time for disengaging attention or reorienting to the actual target position. These findings agree with those of Buchholz & Davies (2005), who, using another variant of the covert orienting task, demonstrated that dyslexic adults showed a cost in shifting attention to the periphery when targets were invalidly cued. Also, on a task in which participants had to react to a target appearing in a rapid stream of distracters (Rapid Serial Visual Presentation task), dyslexics have been found to have difficulty disengaging attention from the rapidly presented stimuli (Hari et al., 1999).

In the present study, participants with ADHD performed more inaccurately and variably than controls with most variability in response time being shown in the valid condition. Higher response variability in ADHD has repeatedly been described (for a review see Klein et al., 2006). Among other factors, it has been related to motor output problems and state instability (Van der Meere, 2005).

Studying only performance measures, however, may not be informative about possible group differences in early orienting and later processing stages, as they only reflect the product of processes preceding the overt response. These processes are reflected by the event-related potentials we investigated, and for which differential effects were revealed for dyslexia and ADHD problems.

In participants with dyslexia (dyslexic and comorbid participants) the early N2 related to processing of the cue was attenuated, especially in the right hemisphere. Moreover, the LORETA solution showed that the activity during presentation of the cue could be localised to the superior parietal lobe (SPL) and precuneus, the latter corresponding with the POZ electrode site. At this site amplitude of the cue N2 was attenuated due to dyslexia problems. Activation of the precuneus has previously been related to processing of spatial cues (Giesbrecht et al., 2003) and attention shifting (Nagahama et al., 1999), which supports the suggestion that these processes may be deficient in our dyslexic participants, with or without co-occurring ADHD. Problems with attention shifting in dyslexia have also been related to poorer functioning of the magnocellular division of the visual system which has major projections to the posterior parietal cortex (for a review

see Jáskowski & Rusiak, 2005), and which is involved in visuo-spatial orienting (Posner & Peterson, 1990).

For the later-occurring target N2, negativity was greater in the valid condition for the factor dyslexia. Previously, enhancement of the N2 has been associated with processing of conflicting stimuli (Nieuwenhuis et al., 2004; Van Veen & Carter, 2002). In the present task, the invalid condition can be seen as conflicting because cue and target appeared in opposite visual fields, so one would expect a larger N2 in the invalid condition. Yet, why then was this N2 amplitude effect for validity not seen in dyslexics? The following explanation may be considered. Dyslexic and comorbid participants demonstrated an attenuated cue-related N2, which may reflect weaker perceptual processing of the cue, leading to a loss of its facilitating function in processing the validly cued target. Hence, compensatory mechanisms may have been applied to process the target fully at a later stage. These compensatory processes may not have been applied in the invalid condition because of the conflict between cue and target, as reflected by a decline in performance, i.e. slower RT. In participants with ADHD, the target N2 did not show amplitude differences, but a longer latency in the valid condition. This suggests that stimulus discrimination was slower, which may have contributed to the longer overall RT compared to controls.

In the later processing stage, the dyslexic participants in our study showed a right-sided suppression of the P3 across conditions. These findings are in line with previous ERP studies (Taylor & Keenen, 1990), in which children with dyslexia had a smaller P3 than controls. Concerning ADHD, the most prominent finding was the greater amplitude in the parietal region, especially in response to valid right targets (see Figure 7). Our findings agree with those of López and colleagues (2006), who, in a visuo-spatial attention task, found no group differences in the early processing stages related to visual attention and a larger P3 in children with ADHD compared to controls, especially in response to peripheral stimuli. Our findings also agree with those of Harter and colleagues (1988), who, using a somewhat different visuo-spatial attention task, found a larger P3 in their sample of children with ADHD, especially in the right hemisphere. Theses authors speculated that the children with ADHD may have been showing increased responsivity and arousal in response to relevant stimuli. This would be in line with the suggestion that the P3 is driven by noradrenergic input from the locus coeruleus, which plays an important role in arousal regulation (Nieuwenhuis et al., 2005). It would also agree with the explanation of attention problems in ADHD in

terms of poor energetic state regulation (Van der Meere, 2005). However, Kok (2001) characterised interpretation of the P3 amplitude within an energetic framework as problematic, as in the past conflicting results have been found, due to varying task constraints. In our study, dyslexic participants may have been using a different strategy than the ADHD participants. This could have caused differential underlying processes contributing to the greater P3 in ADHD and the smaller P3 in dyslexia.

Dyslexics demonstrated a laterality difference for the P3. Another known correlate of P3 amplitude concerns callosal size and transfer speed (Polich & Hoffman, 1998; Hoffman & Polich, 1999). Evidence has accumulated suggesting a less functional corpus callosum in dyslexia, possibly causing slower interhemispheric transfer rates (Badzakov-Trajkov et al., 2005; Davidson & Saron, 1992; Hynd et al., 1995; Markee et al., 1996) and difficulties in orienting attention to invalidly cued targets (Hines et al., 2002). Conversely, greater interhemispheric transfer times have been found in ADHD (Brown & Vickers, 2004; Rolfe et al., 2007; Roessner et al., 2004).

A combination of performance and ERP measures proved useful in dissociating control from clinical groups and clinical groups from each other. The discriminant function analysis showed that dyslexics could be distinguished by early cue and target processing, and that participants with ADHD could be discerned by later, response related and energetic processes. These results are in line with the hypothesis that dyslexics suffer from early processing deficits and participants with ADHD from later processing difficulties. Comorbid participants were similar to dyslexics in early cue processing, and differed from ADHD in RT, suggesting that information processing problems are not an additive result of both disorders, as can also be seen in Figure 8.

A potential limitation of the present study is the inclusion of male participants only. Future studies should include women with dyslexia and ADHD, as it is uncertain how the current findings apply to them. Another suggestion would be to incorporate an endogenous cueing procedure to tap voluntary attention. Because this study was conducted on adults, differences found in information processing may be indexing compensatory strategies that have evolved over time or effects of neural plasticity. To investigate these developmental effects, more research is recommended including a range of age groups. Furthermore, differences in interhemispheric transfer rates could be additionally beneficial in dissociating ADHD from dyslexia.

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